Précis

Retinitis Pigmentosa (RP) is a group of incurable degenerative diseases of the retina that have a complex molecular etiology. Approximately 100,000 Americans suffer from inherited retinal degenerative RP. More than 100 RP-inducing mutations have been identified in several genes including: rhodopsin, the rod visual pigment; peripherin, a membrane structure protein; and PDEB, the beta subunit of rod cyclic GMP (cGMP) phosphodiesterase. However, the genotype is unknown for the majority of patients. Despite this genetic heterogeneity, there tends to be a common pattern of visual loss in patients with RP. Typically, patients experience disturbance in night vision early in life due to the degeneration of rod photoreceptors. The remaining cone photoreceptors become their mainstay of vision, but over the years and decades, the cones slowly degenerate, leading to blindness. These two phases of degeneration in the visual life of an RP patient may involve different underlying pathogenic mechanisms. Regardless of the initial causative defects, the end results are photoreceptor degeneration. This common pathogenesis pathway provides a target for therapeutic intervention.

To date, there are few available, effective treatments for retinal degenerative disorders. One major challenge is to deliver potential therapeutic agents to the back of the eye, in particular to the retina. The blood-eye barrier prevents the penetration of a variety of molecules to the neurosensory retina in a similar manner to the action of the blood-brain barrier, which exists between the central nervous system and systemic circulation. To overcome this challenge, Neurotech USA, Inc. (Neurotech) developed encapsulated cell technology (ECT), specifically the NT-501-10 and NT-501-6A.02 devices, to enable controlled, sustained delivery of therapeutic agents directly into the intra- ocular fluids and thus providing direct access to the retina. ECT utilizes cells encapsulated within a semi-permeable polymer device that secretes therapeutic factors directly into the vitreous. In addition, ECT devices can be retrieved, providing an added level of safety.

Histopathologic studies have demonstrated the possibility of growth factors, neurotrophic factors, and cytokines as therapeutics for RP. Specifically, ciliary neurotrophic factor (CNTF) has proven to be the most effective in reducing retinal degeneration. Therefore, the use of

implanted NT-501-10 and NT-501-6A.02 devices, which secrete CNTF into the retina, may be beneficial in patients with RP and other retinal degenerative diseases.

This pilot study will assess the ophthalmic and systemic safety, and to some extent efficacy, of the novel intra-ocular NT-501- 10 and NT-501-6A.02 implants in patients with RP and poor visual acuity in one eye. The main purpose of the study is to assess the safety of the NT-501-10 and NT-501-6A.02 implants. Secondary outcomes will include the anterior chamber cell scale and vitreous haze grading to measure inflammation, which may be caused by the implant. Other secondary outcome measures related to potential product performance are visual acuity, visual fields, electroretinograms (ERG), and optical coherence tomography (OCT3) to determine retinal thickness.